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March 19, 2012

The Honorable Margaret A. Hamburg, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Hamburg:

We write to express our significant concern regarding the content and implementation of the "Draft Guidance for Industry and FDA Staff: Commercially Distributed In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only: Frequently Asked Questions" (Draft Guidance Document), issued June 1, 2011, by the Food and Drug Administration (FDA or Agency).

The content of the Draft Guidance Document raises several concerns. The Draft Guidance Document appears to represent a disregard of current law on "intended use". In the Draft Guidance Document, FDA indicates that "actual use" will now be a factor in FDA's analysis of "intended use". The definition of "intended use" is essential to the interpretation of the Federal Food, Drug and Cosmetic Act (FFDCA), from serving as the basis for defining whether a product is a "drug" or "device" to determining whether a product is being marketed off-label. Therefore, this addition of "actual use" as a factor in this analysis has significant consequences for not only in vitro diagnostic products labeled "for research only" or "for investigational use only" but also for all FDA-regulated products.

The Agency appears to further exacerbate this disregard of current law by requiring manufacturers to police end users of their products and halt sales if they know or have reason to know that product use goes beyond research. Prior to the publication of the Draft Guidance Document, the Agency was satisfied with a certification from customers acknowledging that Research Use Only (RUO) products were for research use. However, to comply with the Draft Guidance Document, manufacturers now must conduct surveillance on their customers and stop selling to those customers if the manufacturers know or have reason to know that their customers' use of the product goes beyond research. Therefore, under this requirement, manufacturers, rather than the FDA, would enforce the FFDCA.

We also have concerns regarding the apparent policy shift giving rise to the Draft Guidance Document. The Draft Guidance Document appears to extend the regulatory reach of the FDA into clinical laboratories, which are currently overseen by the Centers for Medicare and Medicaid Services (CMS) under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). The Draft Guidance Document appears to force RUO and Investigational Use Only (IUO) manufacturers to police their clinical laboratory customers so the FDA can further extend its regulatory reach. Instead of extending its regulatory reach, the FDA should respect Congressional intent, focus on its core mission and prevent duplicative efforts, by enabling CMS to enforce CLIA.

FDA's process for implementing this guidance also causes substantial concern. As established above, FDA has made significant policy changes in the Draft Guidance Document. In recent years, the Agency has established the practice of issuing guidance documents where regulation was required under the Administrative Procedures Act, 5 U.S.C. § 551 et seq. (APA), or even statutory authority was required, given the significance of the policy change. This Draft Guidance Document appears to continue that practice.

Finally, we are concerned regarding FDA's rapid implementation of the Draft Guidance Document. Although FDA represented that the document "Contains Nonbinding Recommendations" and is "Draft – Not for Implementation", the FDA cited the Draft Guidance Document in a Warning Letter a mere two weeks after the comment period closed. Given the substantial negative stakeholder comment and the fact that the FDA represented the Draft Guidance Document as nonbinding and not for implementation, we question how and why the FDA implemented the Draft Guidance Document so rapidly.

Because of the numerous concerns raised by the content and implementation process, we request the following information on the Draft Guidance Document by April 9, 2012:

1. Please explain how the utilization of "intended use" in the Draft Guidance Document comports with established legal precedent.
2. Please explain the legal basis for forcing manufacturers to enforce the FFDCA.
3. We are concerned that the definition of "research" in this guidance has been inappropriately narrowed and conflicts with definitions in other FDA guidance documents in the diagnostics area, creating confusion and inconsistency. Please explain how this definition interacts with the previous definition.
4. Why did the Draft Guidance Document not make any accommodation for esoteric tests that may be used for rare diseases or emerging public health threats?
5. The Draft Guidance Document represents a significant departure from prior FDA regulations. The FFDCA and APA require the FDA to promulgate rules instead of issuing guidance documents in order to create legally enforceable regulations. Furthermore, the Supreme Court has held that if an agency wants to amend a legislative rule, it must do so by issuing another legislative rule, not by draft guidance. Please explain how this Draft Guidance Document comports with the APA.

6. Why did the FDA not provide a transition period for companies to come into compliance with the Draft Guidance Document?
7. Please indicate whether, how and when you intend to respond to the public comments received to the Draft Guidance Document, especially since the Agency has already released warning letters citing the document.
8. Given the enforcement action above, please explain how this Guidance Document "Contains Nonbinding Recommendations" and is "Draft – Not for Implementation", as represented by the Agency in the Draft Guidance Document.
9. When does the Agency intend to finalize the Draft Guidance Document?
10. Has FDA conducted an economic impact assessment to determine the effect of these new requirements on laboratories, manufacturers and innovation?

Thank you in advance for your prompt attention to this matter. If you have any questions, or need additional information, please contact Heidi Stirrup with Chairman Pitts at (202) 225-2927 or James Paluskiewicz with Dr. Burgess at (202) 225-7772.

Sincerely,

Joseph R. Pitts
Chairman
Subcommittee on Health

Michael C. Burgess
Vice Chairman
Subcommittee on Health

Cathy McMorris Rodgers

Brian P. Bilbray

cc: The Honorable Fred Upton, Chairman

The Honorable Henry A. Waxman, Ranking Member

The Honorable Frank Pallone, Jr., Ranking Member
Subcommittee on Health